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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,123	10/23/2003	Ivo Franci Eggen	O 2000.662 US D3	1629

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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/693,123	EGGEN ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 28 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 28 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 10/199,805.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see attached sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a preliminary amendment, which was dated on October 23, 2003.

Status of the Claims

2. Claims 1-27 were pending. Applicants canceled claims 1-27 and added claim 28. Therefore, claim 28 is pending and examined on the merits.

Information Disclosure Statement

3. The information disclosure statements filed October 23, 2003 and January 20, 2004, fail, in part, to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 several publications cited therein, lack publication dates or a title (i.e., AR for 10/23/03; AU and AV for 1/20/04), a necessary element for consideration. While the other patent and other publications cited therein, and supplied, therewith, have been considered as to the merits, these three publications have not. Applicant is advised that the date of any re-submission of these citations contained in this information disclosure statement or the submission of the missing element – their publication dates – will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPE § 609 C(1). A copy of the form are attached to this Office Action (e.g., 10/23/03; 12/15/03; 1/20/04; 6/8/04).

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence(s) of the specification or in an application data sheet by identifying the prior application by application number (37 CFR 1.78(a)(2) and (a)(5)). If the prior application is a nonprovisional application, the specific reference must also include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. Here, Applicants' preliminary amendment fails to disclose, for example, the relationship (i.e., continuation, divisional, etc.) of the 10/199,805 application in the first line of the specification. In addition, Applicants' have not shown possession under 35 U.S.C. 112, fist paragraph for larger peptides > 10 amino acids (see written description rejection below) or for the production of a "mixture" of peptides (i.e., a library).

Therefore, the filing date of the instant application is deemed to be its actual filing date, **October 23, 2003**.

Specification

5. The abstract of the disclosure is objected to because it does not allow the public generally to determine quickly from a cursory inspection the nature and gist of the invention. Applicants should amend the abstract so that it corresponds to at least one independent claim. For example, Applicants should describe the currently claimed "peptide or mixture of peptides" instead of the "method" that is set forth in the abstract. See 37 C.F.R. § 1.72. Should Applicants amend the

claims in their next reply, the amended abstract should take into account any further limitations added to the broadest independent claim.

6. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For ***claim 28***, the term "rapid" in line 1 is a relative term that renders the claim indefinite (see MPEP 706.03(d)). The term "rapid" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Here, Applicants merely state in the specification that the claimed process "should be rapid [and] easy to scale up" (e.g., see specification, page 1, line 26), but fail to state how rapid the process should be relative to existing technologies.

B. ***Claim 28*** recites the limitation "the process" in the line 2. There is insufficient antecedent basis for this limitation in the claim. The Examiner recommends, "using a process" for replacement.

C. ***Claim 28*** recites the limitation "activated carboxylic functions" in steps (b) and (b'), which lacks antecedent basis. The claim previously refers to "activate carboxylic components" in step (a). The Examiner recommends replacing "functions" with "components."

D. For **claim 28**, the phrase "optionally, (d) a separate deprotection step, followed by one or more aqueous extractions, wherein the process comprises at least one step (b), referred to as step (b') ..." is vague and indefinite because it is not clear what the word "optionally" modifies. For example, the term "optionally, could refer to just step (d) or, alternatively, step (d) + one or more aqueous extraction. In addition, the "optional" step could refer to all three steps (i.e., step (d) + one or more aqueous extraction + the step (b')). Applicants are requested to clarify and/or correct.

E. For **claim 28**, the term "latent anion" is vague and indefinite. When viewed in light of the specification, this terminology is unclear and confusing. This is due to the fact that a "latent anion" is not defined in the specification and compounds such as 3-dimethylamino-1-propylamine appear to be encompassed by this term (e.g., see specification, Example 1, 3rd cycle).

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 28 is rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

Applicants' claims are directed to a peptide or a mixture of peptides produced by the recited method steps (i.e., product-by-process claims) wherein said process steps do not limit they type of peptide or mixture of peptides that can be produced in any material way (e.g., the peptides could be of any length or any sequence).

In contrast, Applicants' specification provides examples of only "small" peptides i.e., 10 amino acids (e.g., see Example 1 showing synthesis of a 4-mer; see also Example 2 showing synthesis of and 8-mer; see also Eggen et al., "Rapid solution-phase synthesis of a 20-mer peptide according to the DioRaSSP method" Chemistry Today/Chimica Oggi 2005; 23 (supplement), pages 21-24, especially page 21, abstract wherein Applicants admit that they had not produced any large peptides as of the filing date of the instant application, "While the method was hitherto merely applied in the synthesis of peptides of a relatively short length [i.e., as of 2005 only short peptides were produced using the claimed method], its applicability in the synthesis of longer peptides was now [i.e., as of 2005] demonstrated"). Furthermore, Applicants state in detail while larger peptides were not previously expected

(e.g., see entire document, especially page 23 paragraph 1 wherein various challenges associated with larger peptides are described), which is presumably the motivation for publishing the 2005 article.

Applicants are referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding adequate disclosure. For adequate disclosure, like enablement, requires representative examples and/or species, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention.* See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. In addition, when there is ***substantial variation within the genus***, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05). Here, Applicants fail to set forth a "representative" number of examples and/or species especially with regard to larger peptides i.e., > 10 amino acids (e.g., see specification, Examples 1 and 2, see also Eggen et al., page 21, abstract wherein Applicants admit that the claimed techniques were not previously applied to larger peptides).

Thus, applicants have not demonstrated in "full, clear, concise, and exact terms" that they are in possession of the claimed invention. Furthermore, the general knowledge and level of skill in the art do not supplement the omitted description because, according to

Applicants' own admission, larger peptides were not contemplated until 2005 because of the apparent unpredictability in the art with regard to their synthesis (e.g., see Eggen et al., abstract; see also page 23, paragraph 1). That is, Applicants explicitly state that the "applicability" of the claimed method had not been accomplished (i.e., possession of the claimed invention) until 2005 Eggen et al. paper (e.g., see Eggen et al., abstract, "While the method was hitherto merely applied in the synthesis of peptide of a relatively short length, its applicability in the synthesis of longer peptide was now demonstrated with the preparation of a protected 20-mer precursor of VIR-576"). Furthermore, it should be noted that the present application does not describe any larger peptide (i.e., > 10 amino acids in length) like the VIR-576 disclosed in the 2005 Eggen et al. reference. It is well settled that claiming only a result (e.g., a peptide of any length) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result, far beyond those means actually discovered or contemplated by the inventor (e.g., peptide < 10 amino acids), so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217 ; *Siegel v. Watson*, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119.

Claims Rejections – 35 U.S.C. 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 28 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Carpino et al. (Carpino et al., "The 1,1-Dioxobenzo[b] thiophene-2-ylmethyloxycarbonyl (Bsmoc) Amino-Protecting Group" *J. Org. Chem.* **1999**, *64*, 4324-4338) (10/23/03 IDS reference AR).

For ***claim 28***, Carpino et al. (see entire document) disclose many peptides (and methods for their production) that anticipate the claimed invention (e.g., see Carpino abstract; see also figure 1 wherein Toxin #2 is disclosed with amino acid sequence Val-Lys-Asn-Gly-Tyr-Ile; see also page 4329, column 2 wherein octapetpide 20 is disclosed; see especially scheme 1 wherein a general scheme for synthesizing a "Deblocked

peptide" is disclosed using Bsmoc "Rapid" continuous solution phase methods. In addition, Carpino et al. disclose Applicants' claimed method steps for producing said peptide or mixture of peptides. For example, Carpino et al. disclose **(a)** a coupling step, using an excess of an activated carboxylic component to acylate an amino component (e.g., see Carpino et al., page 4329, scheme 1 wherein H-AA_1-OR is coupled to an excess of Bsmoc-AA_2-OH to form Bsmoc-AA_2-AA_1-OR using HATU and DIEA, the excess Bsmoc-AA_2-OH is removed by the $NH_2(CH_2CH_2)_3N$; see also page 4327, middle paragraph, "A second byproduct, derived from excess acylating agent, is the amide 16"). Carpino et al. further disclose **(b)** quenching the reaction with a scavenger to remove residual activated carboxylic acid and also using said scavenger to deprotect the growing peptide (e.g., see Carpino et al., page 4329, scheme 1 wherein the Bsmoc protecting group and the excess AA_2 are removed; see also page 4327, compounds 15 and 16). Carpino et al. also disclose **(c)** the use of one or more aqueous extractions to remove the excess activated carboxylic acid compound and Bsmoc protecting groups (e.g., see page Carpino et al., 4329, scheme 1 showing removal of water soluble side products; see also page 4327, middle paragraph; see also abstract, "Application [of Bsmoc amino-protecting groups] ... represents a significant improvement over the corresponding Fmoc-based method for rapid solution synthesis due to the opportunity to use water or saturated sodium chloride solution rather than an acidic phosphate buffer to remove [i.e., extract] all byproducts"). Carpino et al. also disclose repeating steps (a)-(c) above to synthesize a full length peptide and/or protein (e.g., see page 4329, wherein "additional cycles" are disclosed; see also experimental section wherein longer peptides are produced). Finally,

Carpino et al. also disclose the "optional" step (e.g., see 35 U.S.C. 112, second paragraph rejection above) using a "free anion or a latent anion" scavenger (e.g., see page 4329, column 1, first paragraph wherein "ethanolamine" is disclosed. Ethanolamine possesses a free anion or a latent anion" via the following equilibrium in water $NH_2CH_2CH_2OH \leftrightarrow NH_2CH_2CH_2O^- + H^+$ ($pK_a \sim 16$) and thus is amendable to basic aqueous extractions (e.g., Bsmoc-$NHCH_2CH_2OH$ + Base- → Bsmoc-$NHCH_2CH_2O^-$ or $HAA_2NHCH_2CH_2OH$ + Base- → $HAA_2\dot{N}HCH_2CH_2O^-$). Alternatively, the "optional" separate deprotection step, followed by one or more aqueous extractions, wherein the process comprises at elast one step (b), referred to as step (b'), in which an amine comprising a free anion or a latent anion is used as a scavenger of residual activated carboxylic functions has not been afforded any patentable weight. "Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed" (e.g., see MPEP § 2111.0

Alternatively, *assuming arguendo* that the process steps are not anticipated by Carpino et al. (which is not the case, see above), the product of Carpino et al. would still anticipate the claimed invention because the peptide products described in the Carpino et al. reference meet all of the structural limitations of the claimed product (see above) except for the product-by-process limitations (i.e., steps (a)-(d) in claim 28) and thus would either anticipate or render obvious the claimed peptide. See MPEP § 2113, "'[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-

process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.' *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)." Here, Applicants' claims are drawn to a peptide or a mixture of peptides (i.e., a product), but are defined by various method steps that produce said library (i.e., method steps (a)-(d) in claim 28) and, as a result, represent product-by-process claims. Thus, the process limitations do not appear to provide any patentable weight to the claimed invention in accordance with MPEP § 2113. One of ordinary skill would expect the product to be the same no matter how it was synthesized and/or prepared.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
August 24, 2006

JON EPPERSON, PH.D.
PATENT EXAMINER